



Effectiveness of naltrexone in the double blind placebo controlled clinical trial of naltrexone and guanfacine for heroin dependence

V. Palatkin¹, E. Krupitsky², E. Zvartau³, E. Blokhina¹, N. Bushara¹, A. Tyurina¹, E. Verbitskaya¹

1-Pavlov State Medical University, Valdman Institute of Pharmacology, St. Petersburg, Russia

2-St. Petersburg Bekhterev Research Psychoneurological Institute, Department of Alcohol and Drug Addiction, St. Petersburg, Russia

3-Pavlov State Medical University, Administration, St. Petersburg, Russia

Introduction:

- Opiate receptor antagonist naltrexone is approved for relapse prevention in patients with opiate dependence in Russia
- Naltrexone has no effects on the symptoms that may provoke relapse among recently detoxified opiate addicts such as stress, craving, and impulsiveness
- Alpha-adrenoreceptor agonists can reduce the severity of these symptoms and, in turn, improve effectiveness of treatment of opioid dependence with naltrexone
- Combination of naltrexone and adrenoreceptor antagonist guanfacine might reduce the sensitivity to stressful factors, including those factors which provoke exacerbation of craving for opiates, and may reduce the frequency of relapses.

Verification of this hypothesis was the aim of this study.

Methods:

- The randomized double blind placebo controlled study with double masked in parallel groups of patients.
- 244 heroin addicts who recently completed detoxification and gave informed consent were randomized to into one of four treatment groups.

«Four cell study design»

	Guanfacine (G)	Placebo Guanfacine (PG)
Naltrexone (N)	61	62
Placebo Naltrexone (PN)	60	61

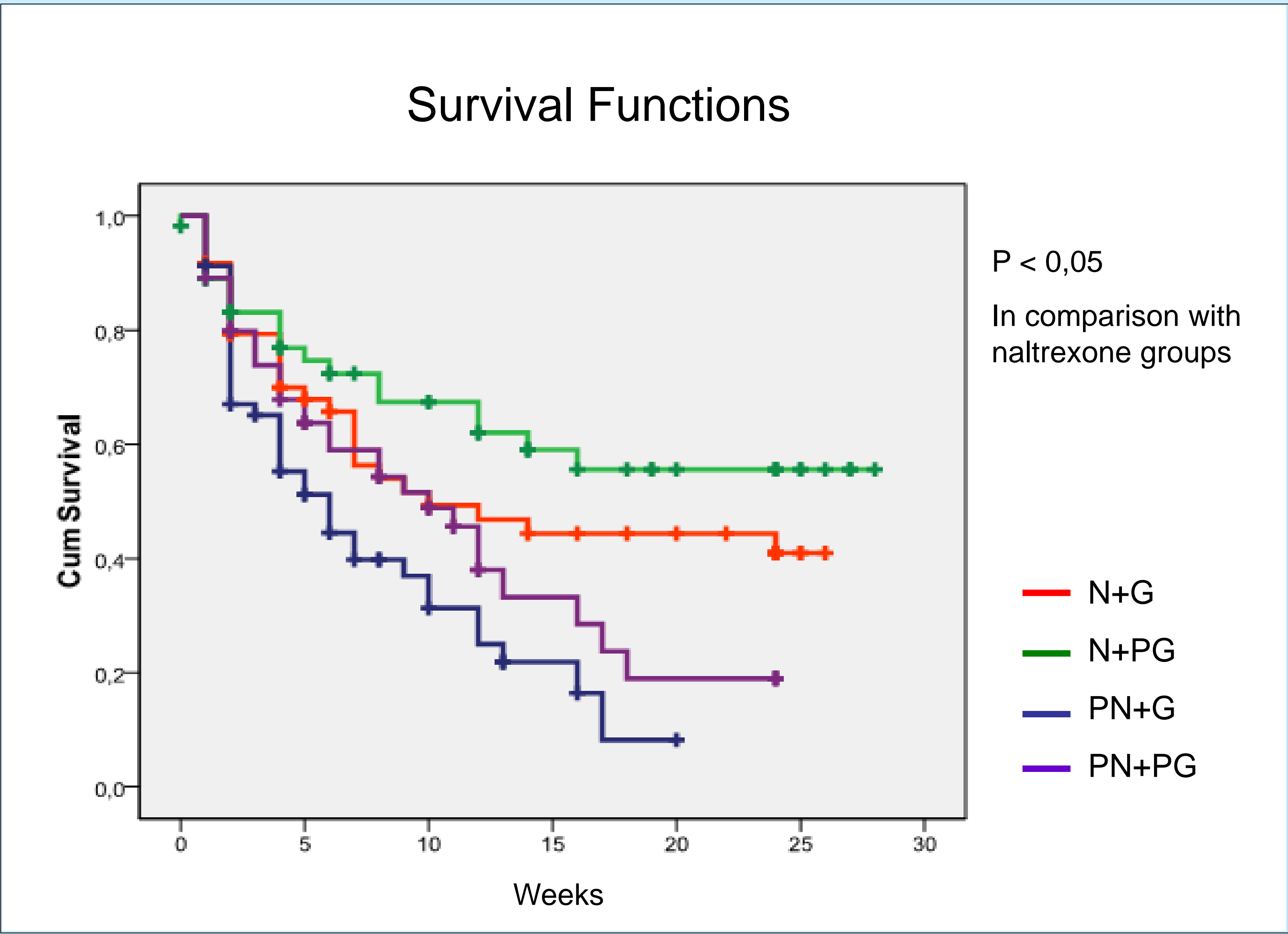
- The duration of the treatment was six months
- Study drugs accepted every day (Naltrexone 50 mg/day and Guanfacine 1 mg/day)
- Bi-weekly visits to the clinic for psychometric evaluation and individual drug counseling
- The control of adherence to N or NP was performed by using urine riboflavin marker
- The control of abstinence was performed by using urine drug strip testing (bi-weekly)
- Patients passed a naloxone challenge for relapse diagnostics. This made always, when a test for opiates in urine was positive
- Evaluation of clinical status and social functioning was performed using international psychometric scales (bi-weekly and then at 3 and 6 month after the end of the study).
- Laboratory diagnostics

Results:

Characteristics of participants

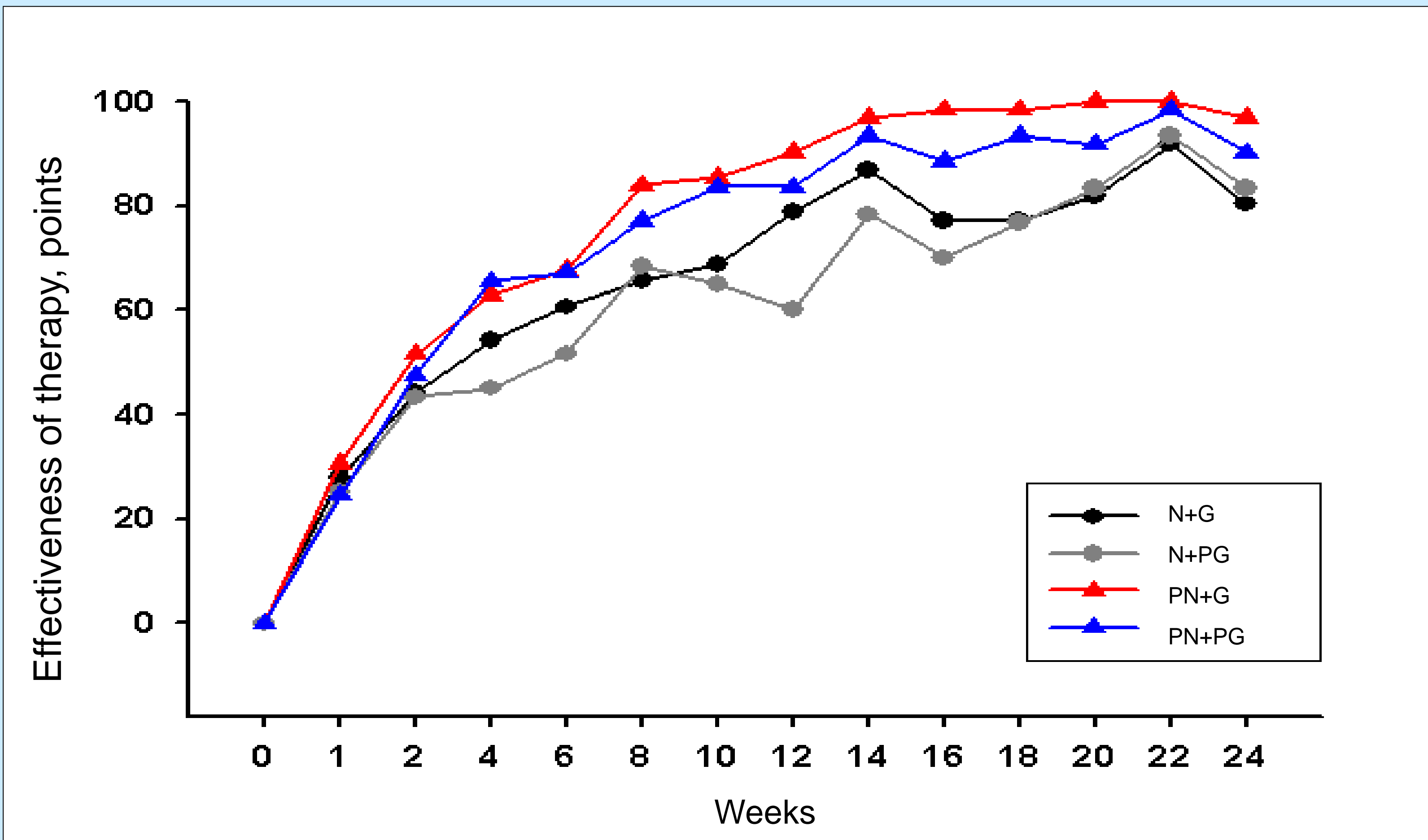
		Groups				Total
		N+G	N+PG	PN+G	PN+PG	
Sex (female)	%	16,4%	18,3%	19,4%	21,3%	18,9%
age	years	26,96	27,95	27,86	27,79	27,64
HIV infection	N	25	24	35	34	118
	%	42,4%	40,0%	56,5%	57,6%	49,2%
Hepatitis B	N	9	12	19	12	52
	%	15,3%	20,3%	30,6%	20,3%	21,8%
Hepatitis C	N	59	57	59	58	233
	%	96,7%	95,0%	95,2%	96,7%	95,9%

Remissions (on treatment groups) Kaplan-Meier Survival Functions



Rating the effectiveness of therapy

Number of missed visits +
Number positive urine test for opiates



Conclusion:

- The efficacy of combination of naltrexone and guanfacine was comparable with efficacy of naltrexone alone
- Usage of combination of opioid receptor antagonist and alpha-adrenoreceptor agonist was safe and associated with low proportion of adverse events

References:

1.Sinha, R., Kimmerling, A., Doebrick, C., Kosten, T.R., 2007 Effects of lofexidine on stress-induced and cue-induced opioid craving and opioid abstinence rates: preliminary findings. *Psychopharmacology (Berl)* 190(4), 569–574.

Supported by NIH # NG-06/1 grant